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The Gut Microbiota Influence Behavior in the Subchronic PCP-induced Model of Schizophrenia

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Introduction: Evidence is accumulating that the gut microbiota (GM) impact on the individual to a degree, which were not previously believed. We investigated the impact of the GM on behavior in the subchronic phencyclidine (PCP) induced model of Schizophrenia.

Materials and methods: Three batches of 24 male Lister Hooded rats, were injected with either PCP (5 mg/kg) or saline twice a day for seven days, followed by seven days wash out. Hereafter the rats were tested in the novel object recognition test and the locomotor activity test, with a timespan of three and six weeks in between for batch two and three, respectively. Fecal samples were collected at relevant time points. The GM was analyzed by denaturation gradient gel electrophoresis, followed by a principal component analysis, and T-tests or regression analysis.

Results: PCP treatment changed the GM up till three weeks after wash out ($p<0.05$) and decreased visual cognition in the same period. ($p<0.05$). Locomotor activity was increased for at least six weeks after wash out. The composition of the GM were strongly correlated to cognitive capabilities in both groups ($p<0.001$ for both). In both groups the GM also correlated to basal activity of the rats, ($p<0.05$ for both), but after an acute injection of PCP in the locomotor activity test, the GM only correlated to behavior in the rats which had previously been exposed to PCP ($p<0.05$).

Conclusion: The study demonstrates an influence of the GM in rats on especially cognitive capabilities, but also on activity. This relationship was evident in the vehicle treated group, but also in the PCP treated group, were the GM composition was changed and correlated to the degree of schizophrenia-like symptoms expressed. The results indicate the relevans of including the variation of the gut microbiota in the analysis of studies using this model.